Human Reproduction Update, Vol.20, No.6 pp. 952–963, 2014

Advanced Access publication on June 16, 2014 doi:10.1093/humupd/dmu030

human reproduction update

Simultaneous prevention of unintended pregnancy and STIs: a challenging compromise

ESHRE Capri Workshop Group[*,†]

*Correspondence address. P.G. Crosignani, Scientific Direction, IRCCS Ca' Granda Foundation Maggiore Policlinico Hospital, Via M. Fanti, 6, 20122 Milano, Italy; E-mail: piergiorgio.crosignani@unimi.it

Submitted on November 21, 2013; resubmitted on May 5, 2014; accepted on May 21, 2014

TABLE OF CONTENTS

- Introduction
- Methods
- Sexual behaviour
- Epidemiology of contraceptive use, unintended pregnancy and STIs
  - Contraceptive use
  - Unintended pregnancy
  - Sexually transmitted infections
  - *Chlamydia trachomatis*
  - Gonorrhoea
  - Syphilis
  - Hepatitis B
  - Hepatitis C
  - HIV/AIDS
  - Human papilloma virus
  - Other STIs
- Contraceptive methods and STIs
  - Barrier methods
  - Hormonal contraceptives
  - Intrauterine contraception
- Simultaneous prevention of unintended pregnancy and STIs
  - Dual method use
  - Simultaneous protection against STI and unwanted conception
- Conclusions and recommendations

BACKGROUND: Unintended pregnancy and sexually transmitted infections (STIs) are the major negative consequences of unsafe sex. Both are common and have long-term social and health consequences. Barrier methods of contraception can prevent both, but unfortunately they are much less effective than the more modern methods at pregnancy prevention. Modern effective contraceptives, however, do not protect against STIs and some may increase the risk of acquisition of infection. This comprehensive review discusses the magnitude of burden of reproductive ill-health, focussing on data from the European region, and explores the relationship between contraceptive use and STIs.

METHODS: Searches were performed by using Medline, Popline, EMBASE, Cochrane Library and the Social Sciences Citation Index databases for relevant English language publications from 1995 to 2012. Summaries were discussed by the European Society of Human Reproduction and Embryology (ESHRE) Workshop Group.

† The list of The ESHRE Capri Workshop Group participants is given in the Appendix.

RESULTS: An understanding of patterns of sexual behaviour helps to understand the epidemiology of unintended pregnancy and STIs and gives pointers towards their prevention, but survey methodologies differ and results are hard to compare. Contraceptive prevalence and method mix vary widely between countries, and the use of the dual method of protection is very infrequent. Abortion rates have fallen in many European countries, particularly Eastern Europe, and contraceptive prevalence increased but unsafe abortion still accounts for 11% of maternal mortality in Eastern Europe. STIs are common but reporting systems are often rudimentary or non-existent and robust data are scarce. Providers still worry about the effect of intrauterine contraception on reproductive tract infections despite reassuring evidence to the contrary. New data on HIV acquisition and hormonal contraception are causing concern in settings where HIV infection is common. New developments in multipurpose technologies aimed at producing a single device/drug, which prevents infection and pregnancy simultaneously, are in early stages. While the benefits of national screening programmes for STIs remain uncertain, human papilloma virus (HPV) vaccination is clearly reducing HPV infection rates and gives hope for the public health benefits of other STI vaccines.

CONCLUSIONS: The consequences of unsafe sex—unintended pregnancy and STI—continue to present major public health problems worldwide even in countries where the prevalence of use of modern contraception is high. Robust systems for routine data collection are sorely needed in most countries and systematic attempts to compare patterns of sexual behaviour across men and women of all ages would be welcome.

Key words: STIs / sexual behaviour / unintended pregnancy / contraception / dual protection

Introduction

At the start of the 21st century, WHO identified unsafe sex as the second most important risk factor for disease, disability or death in the poorest communities and the ninth in developed countries (Ezzati *et al.*, 2002). Unintended pregnancy and sexually transmitted infections (STIs) are the major negative consequences of unsafe sex. Both have significant long-term social and health consequences even in developed countries. Many unintended pregnancies end in induced abortion. In countries where abortion is legal and generally safe, it is nonetheless distressing for all concerned: where abortion is unsafe it is a significant cause of maternal mortality and morbidity. If pregnancy is continued, unintended childbirth is often associated with single motherhood and with reduced life chances for both the mother and her child. STIs increase the risk of infertility, ectopic pregnancy, cervical cancer and, in the case of HIV/AIDS, death (WHO, 2012b). These outcomes of unsafe sex are not independent of one another; women who are at risk of unintended pregnancy may also be at risk of acquiring a STI—and vice versa. Both can be prevented. Unfortunately, methods which prevent STIs (male and female condoms) are not as effective at preventing pregnancy as hormonal and intrauterine contraception, which provide little if any protection against STIs and may in fact be associated with an increased risk of the acquisition or transmission of some infections. All specialists concerned with the sexual and reproductive health of men and women should have a concern about STIs and unintended pregnancy and their prevention, both from an individual patient's perspective and from a public health one.

This paper explores the relationship between contraceptive use and STIs, and the effects of specific methods of contraception on the risks of acquisition or transmission of STIs and their serious consequences. Much of the literature on these two topics comes from the USA or from developing countries and is referred to in the review when relevant or when European data are unavailable. The review draws on European data when available to illustrate the magnitude of the burden on health and to highlight the need for better measurement of both STIs and unintended pregnancy in this part of the world. The paper makes some suggestions for strategies to prevent both STIs and unintended pregnancy.

Methods

For this general review, searches for relevant English language publications from 1995 to 2012 were performed by individual participants in the workshop using Medline, Popline, EMBASE, Cochrane Library and the Social Sciences Citation Index databases. Subject summaries were presented to the European Society of Human Reproduction and Embryology (ESHRE) Workshop Group, where omissions or disagreements were resolved by discussion.

Sexual behaviour

Since they are important in determining fertility and transmission of STIs, sexual behaviour contributes substantially to the burden of disease. Data on sexual behaviour come from surveys which use different methodologies, but all rely on self-reporting. More surveys, and more standard measures, are available for developing countries for which data are collected through repeated Demographic and Health Surveys (Wellings *et al.*, 2006). Data are much harder to find for developed or middle-income countries, and where they are available they are difficult to compare. Questions common to almost all sexual behaviour surveys—and allowing at least some comparison—relate to age at first sex and contraceptive use. Much of the interest in adolescent sexual activity relates to the relatively high incidence of STIs and unintended pregnancy among teenagers, the issues of morality which this raises in many countries and the need to improve patterns of use of condoms and other methods of contraception. One study which analysed data from surveys of sexual behaviour from 59 countries around the world reported a comparison between five European countries: the UK, France, Italy, Norway and Switzerland (Wellings *et al.*, 2006). This showed some differences between countries in the median age of first sex and in the percentage of boys and girls reporting having sex *before* the age of 15 (Table I; Wellings *et al.*, 2006). Data for Europe as a whole are limited to the WHO multi-country Health and Behaviour in School Age Children (HBSC) survey undertaken among 15-year-old students. That survey offers a unique opportunity to explore regional patterns of early sexuality in Europe (Currie *et al.*, 2004, 2012). The proportion of sexually experienced girls has held relatively constant over the last decade (24% ever had sexual intercourse at

Table I Early sexual activity in five European countries (adapted from Wellings *et al.*, 2006).

Country	Median age first sex (women)	Median age first sex (men)	% sex before age 15 (women)	% sex before age 15 (men)
UK	17.5	16.5	6.9	12.5
France	18.5	17.5	5.9	7.2
Italy	18.5	17.5	2.8	4.0
Norway	17.5	18.5	9.6	5.5
Switzerland	18.5	18.5	3.4	6.8

Table II Use of contraception (%) including method mix among European regions (United Nations, 2010).

European region (TFR 2012)	Any method	Any modern method	Female sterilization	Male sterilization	Pill	IUD	Condom	Fertility awareness	Withdrawal
Eastern (1.41)	74.9	54.3	0.9	0.2	11.6	16.3	22.2	9.1	10.4
Northern (1.86)	80.1	77.2	6.1	12.3	22.0	11.9	20.9	1.2	1.5
Southern (1.43)	63.8	46.3	4.6	2.4	16.1	5.7	17.6	2.5	14.4
Western (1.64)	71.9	68.6	4.6	1.7	46.5	11.4	4.8	2.1	0.8

TFR, total fertility rate; IUD, intrauterine device.

age 15), with figures ranging from 17% in Central and Eastern Europe to 36% in Northern Europe.

Epidemiology of contraceptive use, unintended pregnancy and STIs

Contraceptive use

Globally, the total fertility rate (TFR) fell by 29% between 1994 and 2012 and the contraceptive prevalence rate (CPR) among women 15–49 years who are married or in union increased from 58.4 to 63.6%, a rise of ~10% (United Nations, 2012). Trends in contraceptive behaviours in Europe reported from 1997 to 2007 show significant progress in the use of modern methods in Eastern and Northern Europe, but a slight reduction in Southern and Western Europe (United Nations, 2010). The CPR across the European regions varies from 64% in Southern to 80% in Northern Europe (Table II; United Nations, 2010). These regional patterns hide big differences between individual countries within the same region. So, for example, use of the oral contraceptive pill (OC) in the Eastern European region varies from 3.4% in Poland to 39.4% in Hungary; while in Western Europe intrauterine device (IUD) use ranges from 5.3% in Germany to 22.7% in France; and in Southern Europe 3.5% of couples in Portugal rely on withdrawal while in Albania withdrawal accounts for over 57.9% of contraception.

Although the data are available for a limited number of countries only, unmet need for contraception varies substantially, from <4% in Western European countries to 10% or more in Southern and Eastern Europe. Concurrently, the proportion of women using very effective methods (hormonal, IUD and sterilization) increases from 29% in Southern Europe to 64% in Western Europe (United Nations, 2010). The use of condoms at last intercourse has increased from 70 to 78% among young girls between 2000 and 2010 and has remained stable among boys (80 and 81%). Among adolescents condom use varies little by region, while the use of the pill varies significantly from an average of 12% in Eastern Europe to 45% in Western Europe (Currie *et al.*, 2012). Condom use tends to be lower in countries with high use of oral contraception (Fig. 1).

Unintended pregnancy

Unintended pregnancy rates—which include births as well as induced abortions—represent an important indicator of the quality of family planning policies and programmes. Globally, the absolute number of abortions declined from 45.6 million in 1995 to 43.8 million in 2008 (Sedgh *et al.*, 2012). Unfortunately, information on births is mostly unavailable and, where data do exist, the definition of 'unintended' varies. In France and UK, around one-third of births are reported as unintended, most of which occur while women are using contraception (Bajos *et al.*, 2003; Lakha and Glasier, 2006). A simple, standard measure of unintended pregnancy has been validated for use in the UK and could be adapted for other national surveys to allow comparison of rates of unintended births (Barrett *et al.*, 2004). Abortion rates are often used as a surrogate measure of unintended pregnancy. The availability of abortion varies across Europe Region: almost all countries permit abortion to save the mother's life and 90% to preserve mental/physical health; 88% of countries permit abortion for serious fetal anomaly, or if the pregnancy results from rape or incest. Nearly 80% allow abortion for 'social or economic' reasons, and over 70% offer abortion on request. Abortion is illegal on any grounds in Malta and Andorra, and is severely restricted in Poland and Ireland (WHO Regional Office for Europe, 2014). Even when abortion laws are relatively liberal, there are huge variations in reporting. In some countries with mandatory reporting and where

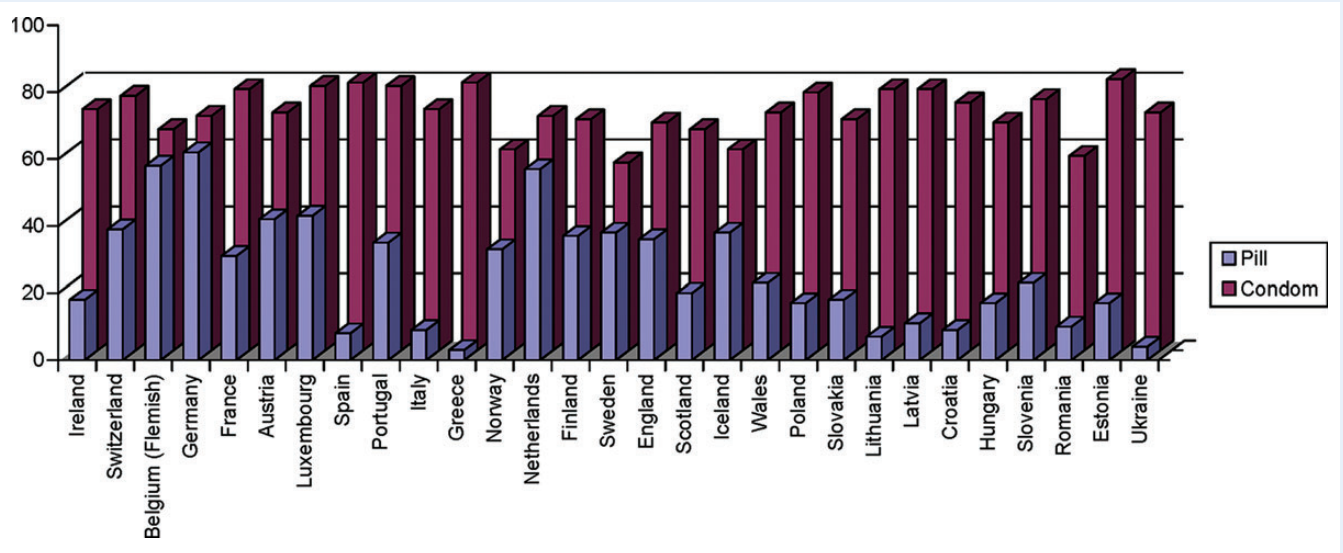

Figure 1 Reported condom and oral contraceptive use % by sexually experienced 15-year-old girls at last sex (from Currie *et al.*, 2012, adapted).

most abortions are undertaken in a public hospital setting (e.g. UK and Sweden), abortion statistics are robust, while in others abortion reporting is poor and the resulting statistics unreliable. Some countries in Western Europe have the lowest abortion rate in the world (12/1000 women of childbearing age). Conversely, Eastern Europe (Belarus, Bulgaria, the Czech Republic, Hungary, Poland, Moldova, Romania, the Russian Federation, Slovakia and Ukraine) has the highest estimated abortion rate in the world. In 2003, there were 103 abortions for every 100 live births. There has nonetheless been a dramatic fall in abortion rates in Eastern Europe—from an estimated 90 per 1000 women of reproductive age in 1995 to 44 in 2004 (Fig. 2). The decline coincided with marked increases in contraceptive use in the region. A disconcerting feature of these disparities remains the occurrence of unsafe abortions in Eastern Europe, responsible for 11% of maternal mortality in the region.

Sexually transmitted infections

The number of annual incident cases of STIs appears to have increased worldwide by 40% since 1995 (WHO, 2012a). This is likely to be a reflection of increased diagnosis and reporting. STIs pose a major public health burden in Europe as they do worldwide. The European Centre for Disease Prevention and Control (ECDC) published a surveillance report on STI epidemiology for the period 2009–2010 (European Centre for Disease Prevention and Control, 2011) which at least gives some idea of the size of the problem and trends. European statistics for the six major STIs are reported in Table III. However, few countries outside North-West Europe have accurate reporting systems for STI. National surveillance systems comprise a mix of voluntary, sentinel or selected laboratory systems and often do not represent true national coverage.

Chlamydia trachomatis

Chlamydia trachomatis is the most frequently reported STI in Europe, but since ~70% of cases are asymptomatic, the rate of 186/100 000 is likely to be grossly underestimated. Reporting in Scandinavia (Sweden, Norway, Denmark and Finland), the Netherlands and the UK accounts for ~95% of all cases of *Chlamydia* infection in Europe. The highest confirmed case rates were reported by Iceland (691 per 100 000), Denmark (505 per 100 000), Norway (464 per 100 000) and Sweden (386 per 100 000). Rates are highest in the 15- to 24-year age group (75% of cases reported). Rates have continued to increase; a doubling of the rate over 10 years reflects increased diagnosis and reporting, including active case finding and in some places screening. Population-based data on the prevalence of STIs are very rare. In a recent large, random British Survey of Sexual Attitudes and Lifestyles (Natsal 3) involving over 15 000 men and women, urine from a sample of sexually active participants was tested for a range of STIs (Sonnenberg *et al.*, 2013). Sixty percent of 8047 eligible participants provided a urine sample. *Chlamydia* prevalence was 1.5% in women and 1.1% in men, but 3.1% in women aged 16–24 and 2.3% in men of that age group.

In Europe, *Chlamydia* infection has arguably attracted the most interest in systematic screening and treatment programmes. A survey of *Chlamydia* prevention programmes in 29 European countries (Low, 2008) found wide variations. Only two countries had national programmes, while almost half reported no organized activity. Countries that have embarked upon, or considered embarking upon national screening programmes for *Chlamydia* infection, face a large amount of missing data. Although all agree that *C. trachomatis* is globally the predominant curable STI, its true incidence and prevalence are, oddly enough, far from clear (Land *et al.*, 2010). In women, *C. trachomatis* is the most frequently involved causative agent of pelvic inflammatory disease (PID), and as such the cause of subsequent tubal subfertility and ectopic pregnancy. Research into the natural history of the disease is severely hampered by the fact that most *Chlamydia* infections remain asymptomatic and thereby escape the attention of the clinician. Colonization of the cervix by *C. trachomatis* may remain unrecognized and does not always lead to serious consequences (Land *et al.*, 2010). Moreover, spontaneous clearance rates of up to 50% have been documented in untreated lower genital tract colonization by *C. trachomatis* (Morré *et al.*, 2002). A positive *Chlamydia* antibody test is suggestive of a prior *C. trachomatis* infection, but does not reflect the course of the disease. If the *Chlamydia* infection is not cleared completely, a persistent infection

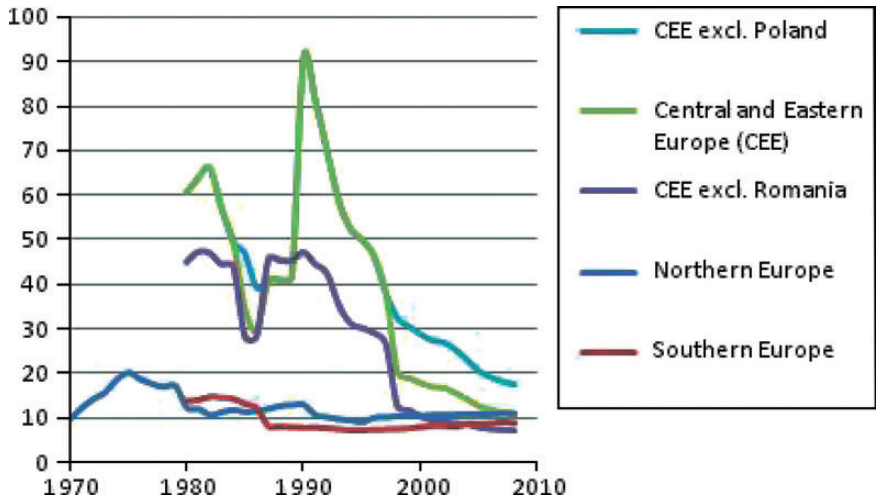

Figure 2 Induced abortions per 1000 women aged 15–49 years in the EU regions in the period 1970–2008 (Gissler *et al.*, 2012).

Table III STI reporting in Europe (European Centre for Disease Prevention and Control, 2011).

Infection	States reporting (*n*)	Total cases (*n*)	Rate/ 100 000	Change since 2006 (%)
Chlamydia	24	344 491	186	↑40
Gonorrhoea	28	31 983	10.4	↓5
Syphilis	29	17 884	4.4	↓50
Hepatitis B	27	14 745	3.4	–
Hepatitis C	26	26 678	6.9	–
HIV/AIDS[a]	28	27 116	5.7[a]	–

[a]Likely to increase due to delayed reporting.

or re-infection may result inducing a chronic low-grade immune response, destroying host cells and increasing the risk of tissue damage, subsequent repair, scarring and adhesion formation. Land *et al.* (2010), in an extensive literature review, estimated the risk of developing PID after a lower genital tract *C. trachomatis* infection at between close to 0 and 30%, depending on the type of test used and the population tested. They calculated the risk of PID processing to tubal subfertility to be between 10 and 20% (Land *et al.*, 2010). This impacts on the appropriateness of (annual) screening programmes for young sexually active women, as proposed by many national guidelines (Low *et al.*, 2009). However, the recent decision reached in the Netherlands following a large randomized trial of three rounds of *Chlamydia* screening—in which screening uptake was low—was *not* to roll out a *Chlamydia* screening programme (Van den Broek *et al.*, 2012).

Gonorrhoea

Reported rates and trends for gonorrhoea vary widely by country; 60% of cases reported in 2010 were from the UK. More than 25% of cases occurred among men who have sex with men (MSM) and 40% in people aged <25. In the Natsal 3 survey in Britain, the population prevalence of gonorrhoea was <0.1% prevalence in both women and men (Sonnenberg *et al.*, 2013).

Syphilis

Syphilis was reported three times more frequently in men than in women (6.6 and 1.8 per 100 000 population, respectively) (European Centre for Disease Prevention and Control, 2011). Fifty-five percent of all reported cases (with data on transmission) occurred in MSM. While in 2010 17% of all syphilis cases were reported in people aged 15–24, most cases were reported among people over age 25. The fall in the rate of syphilis (Table III) is mainly due to a previous 10 years. In contrast, significant increases have occurred in other countries. Congenital syphilis has remained fairly constant [21 countries reported, 59 cases in 2012 (2.5 per 100 000 live births)] (European Centre for Disease Prevention and Control, 2011); however, underreporting is likely to be substantial.

Hepatitis B

Hepatitis B is most likely to affect people aged 25–34 years (33.2% of the total number of cases). The incidence is similar for men (8.79 cases per 100 000) and women (7.42 cases per 100 000) (European Centre for Disease Prevention and Control, 2011). Screening and immunization programmes vary considerably between countries.

Hepatitis C

Similarly, Hepatitis B is most likely to affect people between age 25 and 34 (14.3% of cases: 21.5 per 100 000 in men and 10.3 per 100 000 in women) (European Centre for Disease Prevention and Control, 2011). Surveillance systems, case definitions and testing programmes vary across Europe making comparison between countries difficult.

HIV/AIDS

Although the number of AIDS cases continues to decline—except in some eastern European countries—HIV infection remains a major public health concern. The total number of cases is constant (~28 000

per year), although the epidemiology varies considerably between countries (European Centre for Disease Prevention and Control/WHO Regional Office for Europe, 2012). Estonia has the highest incidence rates, followed by Belgium and Latvia. Rates among MSM (39% of reported infections) increased by 34% between 2004 and 2010, while heterosexually acquired infection (24% of cases) decreased by 25%. Infection in injecting drug users (4%) declined by 40% during the same period, although there were major outbreaks in Romania and Greece. In the Natsal 3 survey in Britain, the population prevalence of HIV infection was 0.1% in women and 0.2% in men (Sonnenberg *et al.*, 2013). Overall in Europe, there has been a 30% decrease in reported AIDS cases, but increases in some Eastern countries. These surveillance data suggest that the HIV epidemic is evolving with diverse transmission patterns across Europe. The number of people living with HIV is increasing as treatment and survival improve. HIV remains highly concentrated in key populations—MSM, people originating from sub-Saharan Africa and injecting drug users. Data from CD4 counts suggest that 50% of diagnoses occur late, reflecting poor access and/or uptake of treatment in many countries.

Human papilloma virus

Data on infection rates with human papilloma virus (HPV) are not routinely reported—indeed, testing in most settings is not routine. More than 150 types of HPV have been described about 40 of which can infect the genital tract. About 70% of cases of cervical cancer are caused by HPV 16 and HPV 18, and HPV types 6 and 11 are responsible for ~90% of genital warts (European Centre for Disease Prevention and Control, 2012). Data on cervical cancer are collected throughout Europe, and each year there are some 33 000 cases and 15 000 deaths. HPV vaccines (Gardasil® and Cervarix®) are safe and highly effective in preventing persistent infection, cervical dysplasia and cancer, but there are few data on efficacy after 9 years.

Most countries in the European region (19/29) now have vaccination programmes for adolescent girls. Ten countries have introduced catch-up programmes for young women (European Centre for Disease Prevention and Control, 2012). However, coverage rates are lower than expected mainly due to expense and the need for three doses over 6 months. Uptake of all three doses in the UK, where vaccination programme started in 2008, is 87%. In the third Natsal survey in Britain (undertaken between 2010 and 2012), prevalence of HPV types 16 and 18 in women aged 18–20 years was lower than in the second survey undertaken in 2000 (5.8 versus 11.3%, respectively) (Sonnenberg *et al.*, 2013). Recent trial data on quadrivalent vaccine (Gardasil®) show that immunogenicity and efficacy are also high in boys. Despite the advantages of vaccinating boys (preventing anal warts, oropharyngeal cancers and cervical cancer through herd immunity), cost-effectiveness models do not favour inclusion of boys in HPV vaccination programmes.

Other STIs

Data on infection rates for other STIs, including trichomonas and herpes, are not routinely reported.

Contraceptive methods and STIs

The only contraceptive methods which prevent against both pregnancy and STIs are barrier methods, specifically male and female condoms. Below we present a summary of the evidence for prevention of both pregnancy and STIs.

Barrier methods

Male condoms

Although the male condom is heavily promoted as the method of choice to reduce the risk of HIV and other STIs, it is considerably less effective than so-called modern methods in the prevention of unintended pregnancy. Latex condoms are impermeable to sperm and to particles the size of most pathogens associated with different STIs; condom failures follow mainly from improper use, inconsistent use or lack of use, rather than from condom breakage or slippage during vaginal sex. The most robust evidence on condom effectiveness concerns the prevention of HIV infection, while information on effectiveness for the prevention of STIs and pregnancy is less convincing. A systematic review of prospective studies on HIV-serodiscordant couples (mostly from Africa) showed that the HIV incidence in couples who always used condoms was 1.14 (95% CI 0.56–2.04) per 100 person-years compared with 5.75 (3.16–9.66) per 100 person-years in those who never used condoms, an ~80% reduction (Weller and Davis-Beaty, 2002). Based on US data from couples desiring pregnancy, about 85 of 100 couples would experience a pregnancy within 1 year of unprotected intercourse (Trussell, 2011). This compares with about 18 pregnancies per 100 couples within 1 year of typical use of male condoms for pregnancy prevention, also an ~80% reduction in risk. In contrast, about 2 in 100 couples using male condoms correctly and consistently in prospective studies would become pregnant within 1 year—an approximate 97% reduction in risk during perfect condom use (Trussell, 2011).

A review of condom effectiveness in 2000 concluded that there was good epidemiological evidence that condoms reduced the risk of gonorrhoea in men (National Institutes of Health, 2001). An updated review in 2004 concluded that condoms reduced the risk of genital HSV-2, syphilis and chlamydial infection in men and women, trichomoniasis in women, and accelerated the regression of cervical and penile HPV-associated lesions and clearance of HPV infection by women (Holmes *et al.*, 2004). The basic concept of the male condom has not evolved over the past 30 years. Non-latex condoms have not shown any advantages over latex condoms, except for people with latex allergies, and condom failure rates have been higher than latex condoms (Callahan *et al.*, 2000; Steiner *et al.*, 2003). Recent innovations include polyurethane strips to assist with correct and rapid application (http://www.sensicondoms.com/) and a folded silicone condom (http://www.origami.com/) currently awaiting regulatory approval.

Female condoms

In a prospective study of the Reality® polyurethane female condom among women from the USA and Latin America, the 6-month pregnancy rate was 15% (Farr *et al.*, 1994). The cumulative annual pregnancy rate for the female condom was extrapolated to 21% under typical use conditions and 5% under perfect use conditions (Trussell *et al.*, 1994). To date, there have been no convincing studies of the comparative effectiveness of female and male condoms for pregnancy or STI prevention, though a randomized study of male and female condom use with a post-coital swab for the presence of prostate-specific antigen showed that some semen exposure occurred more frequently following female than male condom use (22 versus 15%). There was, however, little difference with regard to high levels of post-coital semen detected (5 versus

4%) (Galvao *et al.*, 2005). Innovation in female condoms has been driven by the importance of reducing costs, facilitating insertion and increasing acceptability (Beksinska *et al.*, 2006; Schwartz *et al.*, 2008). It is hoped that availability of more than one product will increase availability and choice of female condoms, which have the advantage of not requiring co-operation of the male partner to be successfully used. However, female condoms have much ground to make up—in 2008, donor countries supplied 18.2 million female condoms globally, compared with nearly 2.4 billion male condoms (Center for Health and Gender Equity, 2011).

Diaphragm

The diaphragm (Ortho-McNeil) used with Replens lubricant gel did not reduce the incidence of HIV infection or STIs in a randomized study in South Africa and Zimbabwe, though participants in the intervention group used fewer (male) condoms than those in the control group (Padian *et al.*, 2007). Recent innovations with the diaphragm include a device which can be loaded with spermicide or lubricant gel on both the cervical and vaginal side (Ballagh *et al.*, 2008), and the one-size fits all SILCS diaphragm (Coffey *et al.*, 2008) now being commercialized in Europe under the brand name Caya™. Comparative effectiveness for pregnancy or STI prevention of these new devices has not been established and all provide for a lubricant or contraceptive gel to be used with the device. While nonoxynol-9 spermicides can be used in settings where women are at no or very limited risk of HIV infection, no safe and effective spermicidal gel has been found that also reduces the risk of infection with HIV or other STIs.

Spermicides

Spermicides are classified with fertility awareness methods as having the lowest contraceptive effectiveness and are estimated to have a typical use annual pregnancy rate of 28% and perfect use pregnancy rate of 18% (Trussell, 2011). Since a double-blind trial showed that nonoxynol-9 spermicide resulted in an increased risk of HIV acquisition (Van Damme et al., 2002), alternative contraceptive products that may protect against HIV and other STIs have been sought. The acid buffering agent BufferGel designed to maintain a vaginal pH of 4 even in the presence of semen was shown in animal models to prevent pregnancy and some other STIs (Barnhart *et al.*, 2007), but not HIV (Abdool Karim *et al.*, 2011).

Hormonal contraceptives

Oral hormonal contraceptives, transdermal patches and vaginal rings when used perfectly have failure rates of 0.3% during the first year of use, while during typical use the failure rate is ~8% (Trussell, 2011). The relationship between hormonal contraception and STD acquisition has been a topic of investigation for many years, though methodological problems (e.g. cross-sectional design and failure to control for potential confounding factors, such as sexual behaviour) have hampered many studies. Hormonal contraceptives provide no protection against STIs. Almost all the data come from studies of oral contraception since patches and rings were developed relatively recently and the number of users worldwide is extremely small. Consistently higher rates of cervical infection with *C. trachomatis* have been found among users of OCs (Cottingham and Hunter, 1992), but the relationship with other STDs is unclear. It has long been suggested that the effect of hormones on thickening cervical mucus may confer some protection against upper genital tract infection and one study (among prostitutes in Kenya) demonstrated that depot medroxyprogesterone acetate (DMPA, depo provera®) use was associated with a significantly decreased risk of PID (Baeten *et al.*, 2001). The overwhelming problem of confounding in all observational studies of STI infection and use of contraception is that condoms prevent against STIs including HIV, and couples who use other contraceptives are less likely to use condoms (Cates and Steiner, 2002). In case–control studies, contraceptive methods that neither increase nor decrease risks of genital tract infection are seen to artificially increase risks when condoms serve as the reference group (Hubacher *et al.*, 2013). However, two serious conditions possibly negatively associated with the use of hormonal contraception are worthy of more detailed discussion—HIV infection and cervical cancer.

Hormonal contraception and HIV/AIDS

Recent research, almost exclusively from Africa, has led to concerns about a relationship between the use of hormonal contraception and HIV infection. A number of animal studies have suggested biological mechanisms by which different hormonal contraceptives may increase the risk of HIV acquisition in women, HIV disease progression or female-to-male HIV transmission (Huijbregts *et al.*, 2013). In 2012, the World Health Organization convened a technical consultation on hormonal contraception and HIV (WHO, 2012b) to review three public health issues:

(i) Acquisition in HIV negative women.
Twenty studies were identified, of which eight cohort studies assessing different hormonal methods met pre-defined minimum quality criteria (Polis and Curtis, 2013). Collectively, the evidence does not establish a clear causal relationship between use of injectable progestogen-only contraceptives and HIV acquisition, but neither does it exclude its possibility.

(ii) HIV disease progression.
Eleven studies were identified which investigated this association—1 randomized clinical trial and 10 observational cohort studies (Phillips *et al.*, 2013). Taken together, the evidence suggests that women living with AIDS can use hormonal contraception without it affecting their risk of disease progression.

(iii) Female-to-male HIV transmission.
Only one cohort study was identified which provided direct evidence about hormonal contraception and the risk of female-to-male transmission of HIV (Polis *et al.*, 2013). Overall, there is insufficient evidence to reach firm conclusions about whether hormonal contraception facilitates female-to-male HIV transmission.

Hormonal contraception, HPV infection and cervical cancer

Oncogenic HPV is the key risk factor for cervical cancer. The global prevalence of HPV is ~10–15%, with however appreciable variations across various populations. HPV prevalence appears to be higher in Eastern Europe, Latin America and sub-Saharan Africa than in other areas of the world (Forman *et al.*, 2012). In North America and Europe, HPV 16 and 18 are the most frequent oncogenic types, while HPV 31, 33, 45 and 58 are relatively common in Africa, Asia and Latin America. Cervical cancer accounts for ~85% of HPV-related cancers, with ~520 000 cases in 2012 (Forman *et al.*, 2013). Most cases (and deaths, i.e. 230 000 in 2012) occur in low- and middle-income countries.

However, factors other than HPV influence cervical carcinogenesis, including cigarette smoking and oral contraceptives (OCs) (La Vecchia and Bosetti, 2003; Cibula *et al.*, 2010; La Vecchia and Boccia, 2014).

The International Agency for Research on Cancer (IARC) conducted a pooled analysis to analyse the combined effect and interactions between HPV and OC on cervical cancer (Moreno *et al.*, 2002). This included 1676 cervical cancer cases and 255 controls from two case–control studies on *in situ* cancers and 8 studies on invasive cancer cervical. There was no significant excess risk for women reporting short-term OC use (<5 years), but the relative risk (RR) was 2.8 for OC use 5–9 years and 4.0 for ≥10 years. HPV positivity was not correlated to OC use among the controls, indicating that OCs do not favour the acquisition or maintenance of HPV infection, but appear to accelerate its progression to cervical cancer. A meta-analysis of 28 studies reported increased cervical cancer risks with longer duration OC use. The RRs were of 1.3–1.6 for 5–9 years and rose to 2.3–2.5 for ≥10 years (Smith *et al.*, 2003). The RRs were apparently of similar magnitude in users of progestogen-only injectable contraceptives, and were consistent across strata of HPV positivity.

The IARC–International Collaboration of Epidemiological Studies of Cervical Cancer (Appleby *et al.*, 2007) gave relevant information on duration and time since stopping OC. That study was based on a collaborative re-analysis of data from 16 573 women with cervical cancer and 35 509 controls without cervical abnormalities. Allowance was made for several relevant covariates, such as age, parity, smoking, age at first intercourse, number of sexual partners and history of screening. The RR was 1.9 (95% CI 1.7–2.1) for current long-term (≥5 years) OC users, but there was no appreciable association for shorter use. The RR, however, declined after stopping use. Consequently, there was no excess risk for ≥10 years since stopping OC use.

In the same collaborative re-analysis, data concerning the use of progestogen-only injectable contraceptives were scanty, but the risk pattern was comparable to that of OC. The pooled RR was 1.22, for users for ≥5 years, but the finding was of borderline significance, and again there was no excess risk for ≥5 years since stopping OC use (Appleby *et al.*, 2007).

Therefore, long-term (i.e. ≥10 years) use of hormonal contraception appears to increase cervical cancer in HPV-positive women. Such an excess risk related to contraception may translate in a cumulative risk at age 50 of ∼0.8% in low- and middle-income countries, and ∼0.4% in high-income countries (Appleby *et al.*, 2007; Cibula *et al.*, 2010). The association between OC and cervical cancer is therefore much more important in low- and middle-income countries, including selected eastern European and Latin America countries, where cervical screening in not adequately utilized, and cervical cancer remains exceedingly high (Franceschi *et al.*, 2000; Bosetti *et al.*, 2005, 2013). Since the risk of mortality and morbidity associated with pregnancy are high in these areas of the world, the benefits of using OCs, even long term, are considered to outweigh the risks, and there is no recommendation to limit OC use to <10 years.

Intrauterine contraception

Intrauterine contraceptives (IUCs) belong to the most effective contraceptive methods with failure rates of 0.1% and no opportunity for imperfect use (Trussell, 2011). The highest use is still seen in China, but IUCs of various types such as copper IUDs (Cu-IUD) or the levonorgestrel-medicated device (LNG-IUS) have become popular in many European countries over the past decades (Gemzell-Danielsson *et al.*, 2011). A persistent barrier to IUC use, however, is the wide-spread belief (among both potential users and providers) of an increased risk for PID among IUC users. Following the discovery in 1977 that the multifilament threads of the Dalkon Shield IUC increased the risk for PID, a FDA subcommittee decision resulted in the recommendation that IUC product labels should include a warning on an increased risk of PID with IUC use (Hubacher *et al.*, 2013). Two large studies estimated a 60% (Burkman, 1981) and, a 10-fold (Vessey *et al.*, 1981) increased rate of PID among IUC users compared with women using other contraceptive methods, and the idea that the IUD caused PID was 'confirmed'. The dogma began to be questioned and in 1992 WHO published an analysis of data from over 51 000 years of observation of 22 908 IUD users. The estimated average PID rate from these studies was only 1.6 per 1000 women-years, but a higher risk (7 per 1000 women-years) was observed within the first month of insertion (Farley *et al.*, 1992). Following this, a study randomizing women to prophylactic antibiotic or placebo treatment prior to IUD insertion showed no difference with regard to PID between the groups (Walsh *et al.*, 1998). Despite evidence that PID is caused by microorganisms transferred at sex or instrumentation of the uterus, there is still a common misunderstanding that PID is caused by the IUC. Sexually transmitted bacteria and non-sterile instrumentation may cause PID. However, it is also clear that exposure to sexually transmitted bacteria not always result in a PID. Untreated *Chlamydia* or gonorrhoea infection will result in PID in <50% of exposed women (Grimes, 2000; Mohllajee *et al.*, 2006). In a small but imaginative study, women were recruited to have an IUD inserted at various intervals prior to hysterectomy (Mishell *et al.*, 1966). Samples were collected from the upper genital tract for bacterial cultures. The findings confirmed that bacteria were present in the uterine cavity following the IUD insertion, but cleared after the next menses following insertion. Taken together, available data indicate that 0–5% of women with an IUD and exposed to bacteria will develop PID (Mohllajee *et al.*, 2006). This can usually be successfully treated with the IUD in place.

There is evidence that the type of IUC may influence the risk of bacterial exposure resulting in PID. Theoretically, the gestagen influence of the LNG-IUS on the cervical mucus may protect against intrauterine transmission of STI agents (Gemzell-Danielsson *et al.*, 2011), while the copper in the Cu-IUD has a bacteriostatic effect. The possible protection against transmission of pathogens as well as the reduced vaginal bleeding associated with the LNG-IUS together with its high contraceptive efficacy may make it a suitable contraceptive method for women living with HIV/AIDS (Heikinheimo *et al.*, 2011). A number of demographic and socioeconomic factors such as age, partnership, education, parity and smoking appear to be associated with PID acquisition (Viberga *et al.*, 2006) The IUC–PID relationship is complex and PID diagnosis frequently imprecise. Great care has to be taken to avoid incorrect conclusions, to correct myths, to update guidelines, to promote effective and safe types of IUC and to help women gain access to intrauterine contraception.

Simultaneous prevention of unintended pregnancy and STIs

There are two approaches aimed at preventing both infection and pregnancy simultaneously—dual method use and the development of multipurpose prevention technologies (Harrison and Shields, 2010).

Dual method use

Currently, available methods of contraception which are most effective at preventing pregnancy do not protect against STIs, whereas condoms which do protect against STIs are less effective at preventing pregnancy. Promotion of condom use is often associated with relatively high pregnancy rates (Feldblum *et al.*, 2007). This presents a dilemma both for couples deciding which method to use and for healthcare providers advising them since if highly effective pregnancy prevention is required, then dual protection involves using an effective contraceptive method together with a condom. Most individuals and couples make a choice depending on their personal circumstances and priorities. For example, mutually monogamous couples may not be at risk of STIs, while women not in a committed relationship and those who have sex with men who have other partners may be more concerned about the risk of infection than of pregnancy. In most high-income countries, dual method use is infrequent 7% in a study of young women in California (Raine *et al.*, 2003), 14% among Australian women aged 25–30 (Lucke *et al.*, 2009). In countries in sub-Saharan Africa where HIV/AIDs and unintended pregnancy are both common, use of dual protection is similarly low. In a nationally representative survey of young South African women aged 15–24, only 7% of current contraceptive users reported using dual methods (MacPhail *et al.*, 2007). In the HBSC survey of 15-year-old girls in Europe, the use of dual protection ranged from 31% in the Netherlands to just 3.5% in Greece and 2.6% in Estonia (Godeau *et al.*, 2008).

Simultaneous protection against STI and unwanted conception

For couples at known risk of STI, including HIV, products which provide simultaneous protection against infection and unintended pregnancy may be more acceptable among stable couples than products that only protect against infection. There is much enthusiasm for developing multipurpose technologies. One approach is to combine a known contraceptive with a known microbicide or virucide. Research is underway on a vaginal gel containing LNG and a microbicide (Carraguard) for either emergency or continuous contraception (Brache *et al.*, 2007). Barrier methods of contraception that includes male and female condoms or diaphragms could be impregnated with anti-infective agents. Recognizing the problems with consistent and correct use of barrier methods, there is considerable interest in using long-acting delivery systems such as contraceptive vaginal rings or intrauterine systems releasing microbicides. Multipurpose vaccines are also in development and the discovery of potentially suitable antigens for several STI pathogens is progressing, including *Chlamydia*, HIV, HSV, gonorrhoea and trichomonas (Harrison and Shields, 2010).

Conclusions and recommendations

STIs and unintended pregnancies are common everywhere and present major public health problems. Action can be taken better to understand the epidemiology and to identify opportunities for improved prevention strategies (Table IV).

Data are frustratingly scarce or unreliable. Surveys of sexual behaviour are more systematically undertaken in developing countries than elsewhere, but all rely on self-reporting and the results are difficult to compare. With regard to unintended pregnancy, robust reporting systems for induced abortion are lacking even in countries where abortion is legal; and data on unintended pregnancy ending in childbirth are very rare. Efforts to increase contraceptive use and reduce unintended pregnancy, as reflected by rates of induced abortion, have resulted in decreased TFRs worldwide and increased contraceptive prevalence. Yet abortion rates are still worryingly high and up to one-third of pregnancies ending in childbirth may be unplanned. In the developing world, preventing unintended pregnancy would go a long way to reducing maternal mortality and morbidity.

Table IV Actions to improve understanding of sexual ill-health and opportunities for prevention.

Standardized collection of data on induced abortion.
National surveys on unintended births.
Population-based surveys testing for common STIs and sexual behaviour.
Critical evaluation of national STI screening trials.
Health policy changes suggested by the study of HPV vaccination programmes.

National rates of STIs are similarly hard to come by and estimates are usually calculated from laboratory data or STI clinic attendances, both depending on symptomatic men and women attending for treatment. For some infections, there appears to be no data collection. Better data collection including population-based estimates from surveys such as Natsal (Sonnenberg *et al.*, 2013) would help in the design of interventions to decrease unsafe sex and to screen and treat for infection. While routine national screening for STIs may seem desirable, lessons can and should be learned from the trials of national STI screening programmes (for *C. trachomatis*) which have served to highlight how little we know about the natural history of this common infection. Gains are also being made in respect of vaccination against HPV and lessons could be learned from this programme when, and if, vaccines for other STIs become available.

Barrier methods of contraception—particularly the male condom—are effective at protecting against both pregnancy and STIs, but correct and consistent use is challenging, particularly for young people, and dual method use seems unlikely ever to become common. The more (and most) effective methods of contraception do not protect against STIs and some may even increase the risk of acquisition or persistence of infection with, in some cases, serious consequences. Nevertheless, the balance of risk is in favour of use of effective contraception since, even in Europe, unintended pregnancy can have major social and health consequences. New developments in multipurpose technologies aimed at producing a single device or drug which prevents infection and pregnancy simultaneously are highly desirable particularly if they can be made long acting—but they are a long way off.

Acknowledgement

The secretarial assistance of Mrs Simonetta Vassallo is gratefully acknowledged.

Funding

The meeting was organized by the European Society of Human Reproduction and Embryology with an unrestricted educational grant from Institut Biochimique S.A. (Switzerland).

Conflict of interest

None declared.

References

Abdool Karim SS, Richardson BA, Ramjee G, Hoffman IF, Chirenje ZM, Taha T, Kapina M, Maslankowski L, Coletti A, Profy A *et al.*; HIV Prevention Trials Network (HPTN) 035 Study Team. Safety and effectiveness of BufferGel and 0.5% PRO2000 gel for the prevention of HIV infection in women. *AIDS* 2011;**25**:957–966.

Appleby P, Beral V, Berrington de Gonzalez A, Colin D, Franceschi S, Goodhill A, Green J, Peto J, Plummer M, Sweetland S. Cervical cancer and hormonal contraceptives: collaborative reanalysis of individual data for 16,573 women with cervical cancer and 35,509 women without cervical cancer from 24 epidemiological studies. *Lancet* 2007;**370**:1609–1621.

Baeten JM, Nyang PM, Richardson BA, Lavreys L, Chohan B, Martin HL Jr, Mandaliya K, Ndinya-Achola JO, Bwayo JJ, Kreiss JK. Hormonal contraception and risk of sexually transmitted disease acquisition: results from a prospective study. *Am J Obstet Gynecol* 2001;**185**:380–385.

Bajos N, Leridon H, Goulard H, Oustry P, Job-Spira N. Contraception: from accessibility to efficiency. *Hum Reprod* 2003;**18**:994–999.

Ballagh SA, Brache V, Mauck C, Callahan MM, Cochon L, Wheeless A, Moench TR. A phase I study of the functional performance, safety and acceptability of the BufferGel® Duet™. *Contraception* 2008;**77**:130–137.

Barnhart KT, Rosenberg MJ, MacKay HT, Blithe DL, Higgins J, Walsh T, Wan L, Thomas M, Creinin MD, Westhoff C *et al.* Contraceptive efficacy of a novel spermicidal microbicide used with a diaphragm: a randomized controlled trial. *Obstet Gynecol* 2007;**110**:577–586.

Barrett G, Smith SC, Wellings K. Conceptualisation, development and evaluation of a measure of unplanned pregnancy. *J Epidemiol Community Health* 2004;**58**:426–433.

Beksinska M, Smit J, Mabude Z, Vijayakumar G, Joanis C. Performance of the Reality® polyurethane female condom and a synthetic latex prototype: a randomized crossover trial among South African women. *Contraception* 2006;**73**:286–393.

Bosetti C, Malvezzi M, Chatenoud L, Negri E, Levi F, La Vecchia C. Trends in cancer mortality in the Americas, 1970–2000. *Ann Oncol* 2005;**16**:489–511.

Bosetti C, Bertuccio P, Malvezzi M, Levi F, Chatenoud L, Negri E, La Vecchia C. Cancer mortality in Europe, 2005–2009, and an overview of trends since 1980. *Ann Oncol* 2013;**24**:2657–2671.

Brache V, Croxatto H, Sitruk-Ware R, Maguire R, Montero JC, Kumar N, Salvatierra AM, Tejada AS, Cochón L, Forcelledo ML *et al.* Effect of a single vaginal administration of levonorgestrel in Carraguard® gel on the ovulatory process: a potential candidate for 'dual protection' emergency contraception. *Contraception* 2007;**76**:111–116.

Burkman RT. Association between intrauterine device and pelvic inflammatory disease. *Obstet Gynecol* 1981;**57**:269–276.

Callahan M, Mauck C, Taylor D, Frezieres R, Walsh T, Martens M. Comparative evaluation of three Tactylon™ condoms and a latex condom during vaginal intercourse: breakage and slippage. *Contraception* 2000;**61**:205–215.

Cates W Jr, Steiner MJ. Dual protection against unintended pregnancy and sexually transmitted infections. What is the best contraceptive approach? *Sex Transm Dis* 2002;**29**:168–174.

Center for Health and Gender Equity (CHANGE). Female Condoms and U.S. Foreign Assistance: an Unfinished Imperative for Women's Health. Washington, DC: Center for Health and Gender Equity. http://www.genderhealth.org/files/uploads/pepfar_watch/publications/unfinishedimperative.pdf (12 June 2014, date last accessed), 2011.

Cibula D, Gompel A, Mueck AO, La Vecchia C, Hannaford PC, Skouby SO, Zikan M, Dusek L. Hormonal contraception and risk of cancer. *Hum Reprod Update* 2010;**16**:631–650.

Coffey PS, Kilbourne-Brook M, Brache V, Cochón L. Comparative acceptability of the SILCS and Ortho ALL-FLEX® diaphragms among couples in the Dominican Republic. *Contraception* 2008;**78**:418–423.

Cottingham J, Hunter D. *Chlamydia trachomatis* and oral contraceptive use: a quantitative review. *Genitourin Med* 1992;**68**:209–216.

Currie C, Roberts C, Morgan A, Smith R, Settertobulte W, Samdal O, Barnekow Rasmussen V. (eds). *Young People's Health in Context. Health Behaviour in School-Aged Children (HBSC) Study: International Report From the 2001/02 Survey.* Copenhagen: WHO Regional Office for Europe, 2004 (Health Policy for Children and Adolescents, No. 4). http://www.euro.who.int/__data/assets/pdf_file/0003/163857/Social-determinants-of-health-and-well-being-among-young-people.pdf. (10 November 2013, date last accessed).

Currie C, Zanotti C, Morgan A, Currie D, de Looze M, Roberts C, Samdal O, Smith ORF, Barnekow V. (eds). *Social Determinants of Health and Well-Being among Young People. Health Behaviour in School-Aged Children (HBSC) Study: International Report From the 2009/2010 Survey*. Copenhagen: WHO Regional Office for Europe, 2012 (Health Policy for Children and Adolescents, No. 6). http://www.euro.who.int/__data/assets/pdf_file/0008/110231/e82923.pdf. (10 November 2013, date last accessed).

European Centre for Disease Prevention and Control. *Sexually Transmitted Infections in Europe, 1990–2009*. Stockholm: ECDC, 2011.

European Centre for Disease Prevention and Control. *Introduction of HPV vaccines in EU Countries—an update*. Stockholm: ECDC, 2012.

European Centre for Disease Prevention and Control/WHO Regional Office for Europe. *HIV/AIDS Surveillance in Europe 2011*. Stockholm: ECDC, 2012.

Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S, Murray CJL, the Comparative Risk Assessment Collaborating Group. Selected major risk factors and global and regional burden of disease. *Lancet* 2002;**360**:1347–1360.

Farley TM, Rosenberg MJ, Rowe PJ, Chen JH, Meirik O. Intrauterine devices and pelvic inflammatory disease: an international perspective. *Lancet* 1992;**339**:785–788.

Farr G, Gabelnick H, Sturgen K, Dorflinger L. Contraceptive efficacy and acceptability of the female condom. *Am J Public Health* 1994;**84**:1960–1964.

Feldblum PJ, Nasutiona MD, Hokea TH, Van Damme K, Turner AN, Gmach R, Wong EL, Behets F. Pregnancy among sex workers participating in a condom intervention trial highlights the need for dual protection. *Contraception* 2007;**76**:105–110.

Forman D, de Martel C, Lacey CJ, Soerjomataram I, Lortet-Tieulent J, Bruni L, Vignat J, Ferlay J, Bray F, Plummer M *et al.* Global burden of human papillomavirus and related diseases. *Vaccine* 2012;**30**(Suppl 5):F12–F23.

Forman D, Bray F, Brewster DH, Gombe Mbalawa C, Kohler B, Pineros M, Steliarova-Foucher E, Swaminathan R, Ferlay J. (eds). *Cancer Incidence in Five Continents, Vol. X (Electronic Version)*. Lyon: IARC, 2013.

Franceschi S, Herrero R, La Vecchia C. Cervical cancer screening in Europe. What next? *Eur J Cancer* 2000;**36**:2272–2275.

Galvao LW, Oliveira LC, Diaz J, Kim D-J, Marchi N, van Dam J, Castilho RF, Chen M, Macaluso M. Effectiveness of female and male condoms in preventing exposure to semen during vaginal intercourse: a randomized trial. *Contraception* 2005;**71**:130–136.

Gemzell-Danielsson K, Inki P, Heikinheimo O. Recent developments in the clinical use of the levonorgestrel-releasing intrauterine system. *Acta Obstet Gynecol Scand* 2011;**90**:1177–1188.

Gissler M, Fronteira I, Jahn A, Karro H, Moreau C, Oliveira da Silva M, Olsen J, Savona-Ventura C, Temmerman M, Hemminki E; REPROSTAT group. Terminations of pregnancy in the European Union. *BJOG* 2012;**119**:324–332.

Godeau E, Nic Gabhainn S, Vignes C, Ross J, Boyce W, Todd J. Contraceptive use by 15-year-old students at their last sexual intercourse: results from 24 countries. *Arch Pediatr Adolesc Med* 2008;**162**:66–73.

Grimes DA. Intrauterine device and upper-genital-tract infection. *Lancet* 2000;**356**:1013–1019.

Harrison P, Shields WC. Multipurpose prevention technologies for sexual and reproductive health: gaining momentum and promise. *Contraception* 2010;**81**:177–180.

Heikinheimo O, Lehtovirta P, Aho I, Ristola M, Paavonen J. The levonorgestrel-releasing intrauterine system in human immunodeficiency virus-infected women: a 5-year follow-up study. *Am J Obstet Gynecol* 2011;**204**:126.e1–4.

Holmes KK, Levine R, Weaver M. Effectiveness of condoms in preventing sexually transmitted infections. *Bull World Health Organ* 2004;**82**:454–461.

Hubacher D, Grimes DA, Gemzell-Danielsson K. Pitfalls of research linking the intrauterine device to pelvic inflammatory disease. *Obstet Gynecol* 2013;**121**:1091–1098.

Huijbregts RP, Helton ES, Michel KG, Sabbaj S, Richter HE, Goepfert PA, Hel Z. Hormonal contraception and HIV-1 infection: medroxyprogesterone acetate suppresses innate and adaptive immune mechanisms. *Endocrinology* 2013;**154**:1282–1295.

Lakha F, Glasier A. Unintended pregnancy and use of emergency contraception among a large cohort of women attending for antenatal care or abortion in Scotland. *Lancet* 2006;**368**:1782–1787.

Land JA, Van Bergen JE, Morré SA, Postma MJ. Epidemiology of *Chlamydia trachomatis* infection in women and the cost-effectiveness of screening. *Hum Reprod Update* 2010;**16**:189–204.

La Vecchia C, Boccia S. Oral contraceptives, human papillomavirus and cervical cancer. *Eur J Cancer Prev* 2014;**23**:110–112.

La Vecchia C, Bosetti C. Oral contraceptives and cervical cancer: public health implications. *Eur J Cancer Prev* 2003;**12**:1–2.

Low N; SCREen project team. Publication of report on chlamydia control activities in Europe. *Euro Surveill* 2008;**13**. pii: 18924.

Low N, Bender N, Nartey L, Shang A, Stephenson JM. Effectiveness of chlamydia screening: systematic review. *Int J Epidemiol* 2009;**38**:435–448.

Lucke JC, Watson M, Herbert D. Changing patterns of contraceptive use in Australian women. *Contraception* 2009;**80**:533–539.

MacPhail C, Pettifor A, Pascoe S, Rees H. Predictors of dual method use for pregnancy and HIV prevention among adolescent South African women. *Contraception* 2007; **75**:383–389.

Mishell DRJ, Bell JH, Good RG, Moyer DL. The intrauterine device: a bacteriologic study of the endometrial cavity. *Am J Obstet Gynecol* 1966;**96**:119–126.

Mohllajee AP, Curtis KM, Peterson HB. Does insertion and use of an intrauterine device increase the risk of pelvic inflammatory disease among women with sexually transmitted infection? A systematic review. *Contraception* 2006;**73**: 145–153.

Moreno V, Bosch FX, Munoz N, Meijer CJ, Shah KV, Walboomers JM, Herrero R, Franceschi S. Effect of oral contraceptives on risk of cervical cancer in women with human papillomavirus infection: the IARC multicentric case-control study. *Lancet* 2002;**359**:1085–1092.

Morré SA, van den Brule AJ, Rozendaal L, Boeke AJ, Voorhorst FJ, de Blok S, Meijer CJ. The natural course of asymptomatic *Chlamydia trachomatis* infections: 45% clearance and no development of clinical PID after one-year follow-up. *Int J STD AIDS* 2002; **13**(Suppl 2):12–18.

National Institutes of Health, National Institute of Allergy and Infectious Diseases, Department of Health and Human Services. Workshop Summary: Scientific Evidence on Condom Effectiveness for Sexually Transmitted Disease (STD) Prevention. (http://www.niaid.nih.gov/about/organization/dmid/documents/condomreport.pdf) (12 June 2014, date last accessed), 2001.

Padian NS, van der Straten A, Ramjee G, Chipato T, de Bruyn G, Blanchard K, Shiboski S, Montgomery ET, Fancher H, Cheng H *et al.*; MIRA Team. Diaphragm and lubricant gel for prevention of HIV acquisition in southern African women: a randomised controlled trial. *Lancet* 2007;**370**:251–261.

Phillips SJ, Curtis KM, Polis CB. Effect of hormonal contraceptive methods on HIV disease progression: a systematic review. *AIDS* 2013;**25**:787–794.

Polis CB, Curtis KM. Use of hormonal contraceptives and HIV acquisition in women: a systematic review of the epidemiological evidence. *Lancet Infect Dis* 2013; **13**:797–808.

Polis CB, Phillips SJ, Curtis KM. Hormonal contraceptive use and female-to-male HIV transmission: a systematic review of epidemiological evidence. *AIDS* 2013; **27**:493–505.

Raine T, Minnis AM, Padian NS. Determinants of contraceptive method among young women at risk for unintended pregnancy and sexually transmitted infections. *Contraception* 2003;**68**:19–25.

Schwartz JL, Barnhart K, Creinin MD, Poindexter A, Wheeless A, Kilbourne-Brook M, Mauck CK, Weiner DH, Callahan MM. Comparative crossover study of the PATH Woman's Condom and the FC Female Condom®. *Contraception* 2008; **78**:465–473.

Sedgh G, Singh S, Shah IH, Åhman E, Henshaw SK, Bankole A. Induced abortion: incidence and trends worldwide from 1995 to 2008. *Lancet* 2012; **379**:625–632.

Smith JS, Green J, Berrington de Gonzalez A, Appleby P, Peto J, Plummer M, Franceschi S, Beral V. Cervical cancer and use of hormonal contraceptives: a systematic review. *Lancet* 2003;**361**:1159–1167.

Sonnenberg P, Clifton S, Beddows S, Field N, Soldan K, Tanton C, Mercer CH, da Silva FC, Alexander S, Copas AJ *et al.* Prevalence, risk factors, and uptake of interventions for sexually transmitted infections in Britain: findings from the National Surveys of Sexual Attitudes and Lifestyles (Natsal). *Lancet* 2013; **382**:1795–1806.

Steiner MJ, Dominik R, Rountree RW, Nanda K, Dorflinger LJ. Contraceptive effectiveness of a polyurethane condom and a latex condom: a randomized controlled trial. *Obstet Gynecol* 2003;**101**:539–547.

Trussell J. Contraceptive failure in the United States. *Contraception* 2011;**83**:397–404.

Trussell J, Sturgen K, Strickler J, Dominik R. Comparative contraceptive efficacy of the female condom and other barrier methods. *Fam Plann Perspect* 1994;**26**:66–72.

United Nations. Population and Vital Statistics Report. http://www.un.org/esa/population/publications/contraceptive2011/wallchart_front.pdf. (10 July 2010, date last accessed).

United Nations. Department of Economic and Social Affairs, Population Division. *World Contraceptive Use 2012* (POP/DB/CP/Rev2012). 2012

Van Damme L, Ramjee G, Alary M, Vuylsteke B, Chandeying V, Mukenge-Tshibaka L, Ettiègne-Traoré V, Uaheowitchai C, Karim SS, Mâsse B *et al.*; COL-1492 Study Group. Effectiveness of COL-1492, a nonoxynol-9 vaginal gel, on HIV-transmission among female sex workers. *Lancet* 2002;**360**:971–977.

van den Broek IV, van Bergen JE, Brouwers EE, Fennema JS, Götz HM, Hoebe CJ, Koekenbier RH, Kretzschmar M, Over EA, Schmid BV *et al.* Effectiveness of yearly, register based screening for chlamydia in the Netherlands: controlled trial with randomised stepped wedge implementation. *BMJ* 2012;**345**:e4316.

Vessey MP, Yeates D, Flavel R, McPherson K. Pelvic inflammatory disease and the intrauterine device: findings in a large cohort study. *BMJ (Clin Res Ed)* 1981; **282**:855–857.

Viberga I, Odlind V, Lazdane G. Characteristics of women at low risk of STI presenting with pelvic inflammatory disease. *Eur J Contracept Reprod Health Care* 2006; **11**:60–68.

Walsh T, Grimes D, Frezieres R, Nelson A, Bernstein L, Coulson A, Bernstein G. Randomised controlled trial of prophylactic antibiotics before insertion of intrauterine devices. IUD Study Group. *Lancet* 1998;**351**:1005–1008.

Weller SC, Davis-Beaty K. Condom effectiveness in reducing heterosexual HIV transmission. *Cochrane Database Syst Rev* 2002;**1**.

Wellings K, Collumbien M, Slaymaker E, Singh S, Hodges Z, Patel D, Bajos N. Sexual behaviour in context: a global perspective. *Lancet* 2006;**368**:1706–1728.

WHO. *Global Incidence and Prevalence of Selected Curable Sexually Transmitted Infections*. Geneva: World Health Organization, 2012a.

WHO. Hormonal Contraception and HIV. Technical Statement. http://www.who.int/reproductivehealth/publications/family_planning/rhr_12_8/en/ (13 June 2013, date last accessed), 2012b.

WHO Regional Office for Europe. European Health for All Database (HFA-DB). http://www.euro.who.int/hfadb (12 June 2014, date last accessed), 2014.

Appendix

A meeting was organized by the ESHRE (30–31 August 2013) to discuss the above subjects. The contributors included: J.L.H. Evers (Department of Obstetrics and Gynecology, Maastricht University Medical Centre, Maastricht, the Netherlands), T. Farley (Sigma3 Services SARL Scientific & Statistical Solutions, Nyon, Switzerland), K. Gemzell-Danielsson (Chair Division of Obstetrics and Gynecology, Department of Women's and Children's Health Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden), A. Glasier (Centre for Reproductive Biology, University of Edinburgh, UK), P. Hannaford (NHS Grampian Chair of Primary Care and Vice Principal of Research and Knowledge Exchange, Academic Primary Care, Division of Applied Health Sciences, University of Aberdeen, Foresterhill Health Centre, Aberdeen, UK; P. Hannaford prepared the abstract and the slides presented in his absence by A. Glasier. P. Hannaford contributed also to the preparation of the final manuscript), C. La Vecchia (Istituto di Ricerche Farmacologiche 'Mario Negri' and Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milano, Italy), C. Moreau (Population Family and Reproductive Health, Bloomberg School of Public Health, Hopkins University, Baltimore, MD, USA and INSERM U1018, CESP-'Gender, Sexual and Reproductive Health', Hopital du Kremlin Bicetre, Le Kremlin Bicetre, France) and J. Stephenson (Margaret Pyke Professor of Sexual & Reproductive Health, UCL, Programme Director

for Women's Health, UCL Partners, Research Department of Reproductive Health, Institute of Women's Health, University College London, London, UK). The discussants included: D.T. Baird (Centre for Reproductive Biology, University of Edinburgh, UK), P.G. Crosignani (Scientific Direction, IRCCS Ca' Granda Foundation, Maggiore Policlinico Hospital, Milano, Italy) and L. Gianaroli (SISMER, Reproductive Medicine Unit, Bologna, Italy). The report was prepared by A. Glasier and P.G. Crosignani.